REMARKS

Formal Matters

Claims 33-35 and 51-68 were examined and rejected.

Claims 33-35 and 51-68 are reworded to be new claims 69-87 for clarity. Support for new claims 60-67 is found at page 8, lines 3-10; page 9, lines 1-13; page 19, lines 11-21; page 35, lines 1-10; page 4, lines 4-5; page 20, lines 7-10; page 43, lines 21-23 and Example 1, starting on page 20, line 30, of the specification as originally filed. No new matter is added.

Claims 33-35 and 51-68 are cancelled without prejudice.

The rejections outlined in the Office Action of May 9, 2007, are applied to the new claims.

Reconsideration of this application is respectfully requested.

Priority

This application is a continuation of prior application 10/417,820, now abandoned, which application is a continuation of 09/416,760, now abandoned, which application claims the benefit of provisional patent applications 60/152,524, filed September 3, 1999, 60/151,114 filed, August 27, 1999 and 60/108,029, filed November 12, 1998.

Submitted herewith is an Application Data Sheet (ADS) including this priority information.

Submission of an ADS should be sufficient to assert priority. Further M.P.E.P. § 601.05 states that the priority of an application need not be made part of the specification:

> M.P.E.P. § 601.05: "(5) *Domestic priority information.* This information includes the application number, the filing date, the status (including patent number if available), and relationship of each application for which a benefit is claimed under 35 U.S.C. §§ 119(e), 120, 121, or 365(c). Providing this information in the application data sheet constitutes the specific reference required by 35 U.S.C. §§119(e) or 120, and § 1.78(a)(2) or § 1.78(a)(4), and need not otherwise be made part of the specification." (emphasis added).

As such, it is believed that the specification need not be amended to reflect the change in the priority claim.

Rejection of claims under 35 U.S.C. § 112, second paragraph

Claims 33, 34 and 51-54 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite.

It is understood that most aspects of this rejection have been addressed by the provision of a new set of claims.

With respect to the use of the term "partial agonist" in claim 70, the Examiner is reminded according to MPEP § 2173[1], the standard for meeting the requirement for definiteness set forth in 35 U.S.C. § 112, second paragraph, is an objective one that requires an analysis of the specification, the teachings of the prior art, and how the claim would be read by one of one of ordinary skill in the art. Per MPEP § 2173.02, the claims should *not* be analyzed for definiteness in a vacuum.

Since the term "partial agonist" is art-recognized, well used, and explicitly defined in the specification to have a meaning consistent with its art-recognized use, the Applicants believe that its use in the claims should cause no confusion.

Further, the specification as filed provides ATP and ADP as exemplary agonists of endogenous human TDAG8 (see, e.g., page 42, line 4 to page 44, line 3, Fig. 2 and Fig. 4 of the specification). Agonists less able to increase cAMP levels than ATP or ADP are partial agonists.

The Applicants submit that this rejection has been adequately addressed. Withdrawal of this rejection is requested.

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[1] See, e.g., MPEP § 2173.02: "The essential inquiry pertaining to this requirement is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. Definiteness of claim language must be analyzed, not in a vacuum, but in light of:
(A) The content of the particular application disclosure;
(B) The teachings of the prior art; and
(C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made."

Rejection of claims under 35 U.S.C. § 101

Claims 33-35 and 51-68 are rejected under 35 U.S.C. § 101 as allegedly unsupported by a patentable utility. The Applicants respectfully traverse this rejection.

Increasing cAMP levels in peripheral blood leukocytes (PBLs) decreases the production of pro-inflammatory mediators, including platelet activating factor, γ-interferon and TNF, and increases the production of anti-inflammatory mediators, including IL-10[2]. Since the claims are directed to a method of identifying compounds that increase cAMP levels in PBLs, the claims have a clear utility in identifying compounds that have anti-inflammatory activity.

The Applicants submit that this utility is credible, specific and substantial. Since no more is required to meet the requirements of 35 U.S.C. §101, this rejection should be withdrawn.

Rejection of claims under 35 U.S.C. § 112, first paragraph (utility)

Claims 33-35 and 51-68 are rejected under 35 U.S.C. §112, first paragraph, because they are rejected under 35 U.S.C. §101.

The Applicants respectfully submit that this rejection should be withdrawn along with the §101 rejection for the reasons outlined above.

Withdrawal of this rejection is requested.

Rejection of claims under 35 U.S.C. § 112, first paragraph (written description)

Claims 33-35 and 51-68 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that is not adequately described by the instant specification. The basis for these rejections relates in large part to the claims encompassing variants of human TDAG8. The question is whether such variants are adequately described in the specification. This rejection is respectfully traversed.

In response, the Examiner is respectfully directed to Fig. 2 of *Kyaw* (DNA Cell Biol. 1998 17: 493-500) which shows a pairwise alignment of the amino acid sequences of human

[2] See, e.g., Eigler (J. Leukocyte Biology 1998 63: 101-107); Moore et al (Clin. Exp. Immunol. 1995 101: 387-389) and Benbernou (Immunology 1997 91: 361-368). These references were published before the priority date of the instant application.

TDAG8 and mouse TDAG8. *Kyaw* has been provided to the office in the Information Disclosure Statement filed on February 18, 2004. *Kyaw*'s Fig. 2 is shown below:

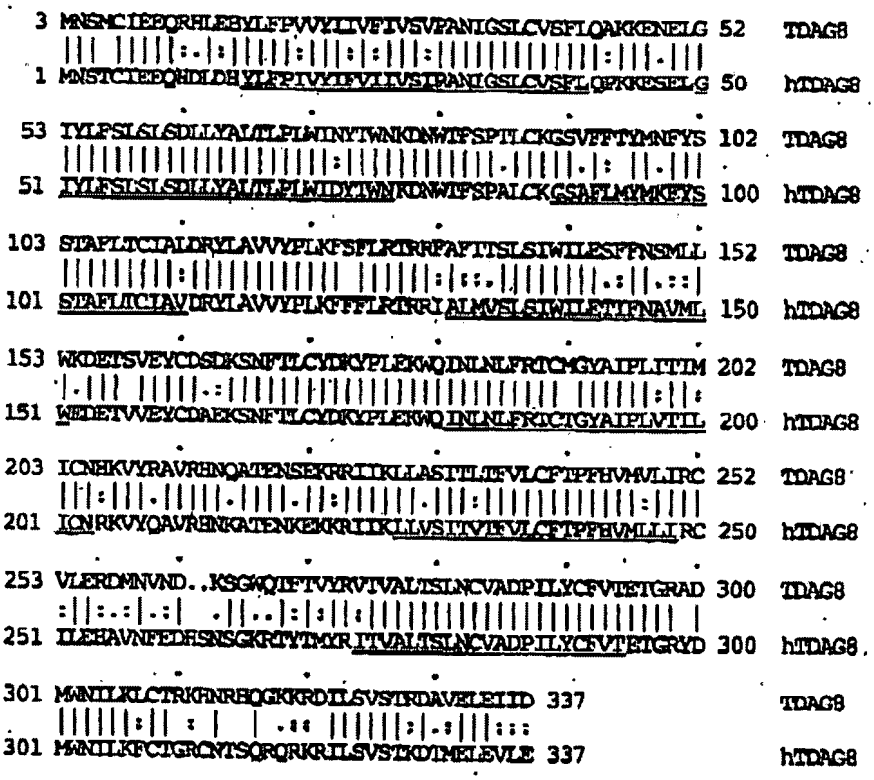


FIG. 2. Alignment of amino acid sequences of the mouse TDAG8 (top) and the hTDAG8 (bottom). Underlined sequences represent the seven putative transmembrane domains of the hTDAG8. The alignment presentation was done with BESTFIT in the GCG package.

According to Kyaw's results section, the mouse and human TDAG8 proteins are about 81% identical, which agrees with the Applicant's calculations. Since the claimed method can be performed with either of these proteins, or any hybrid protein that contains any combination of sequences from the mouse and human proteins, the Applicant submits that one of skill in the art would be able to envision a large number of operable variants of TDAG8.

Further, the Examiner is respectfully referred to:

a) page 2, lines 15 to page 3 line 11, of the instant specification, where the structure/function relationship of GPCRs is described;

b) page 27, line 27 to page 28, line 8, particularly, page 28, lines 5-8, where the amino acid polymorphisms in human TDAG8 are described;

c) page 28, lines 27-31 and Table I on page 42, where the specification provides guidance for making constitutively active mutants of TDAG8; and

d) the section starting on page 35, where a variety of methods for assaying GPCRs (which can be used to test variant proteins) are described in detail.

Also, as shown in Exhibit A, a search of NCBI's PubMed database reveals that there are well over 1275 journal articles, including 172 reviews, that have a publication date that precedes the priority date of the instant application (November 12, 1998) and contain the phrase "GPCR" OR "G protein-coupled receptor" in the abstract. Thus, at the priority date of the instant application, GPCR proteins were a subject of significant interest in the scientific community. The art in which the subject TDAG8 protein belongs was therefore highly developed at the priority date of the instant application.

For example, at the priority date of the instant application, the structure/function relationship of many GPCRs had been investigated, several reviews on the structure/function relationship of GPCRs had been published, algorithms for predicting GPCR structure were available, and many papers that describe the engineering of GPCRs by domain swapping and mutagenesis had been published. Support for this is found in the publications listed in Exhibit B. These publications are supplied herewith in an Information Disclosure Statement.

Given a) the vast amount of available information on structure/function relationships in GPCR proteins in general, b) the availability of the amino acid sequences of human and mouse TDAG8, c) the availability of several amino acid polymorphisms of TDAG8, as well as activating amino acid substitutions; and d) the structure/function information on TDAG8 in the instant specification, the Applicant submits that one of skill in the art would be able to envision a large number of operable variants of TDAG8.

The Applicant understands that the effect of amino acid and nucleotide substitutions cannot be predicted with absolute certainty. However, given the information in the instant specification and the deep general understanding of the structure and function of GPCR proteins, the Applicant submits that such molecules are more than adequately described.

The Applicant submits that these rejections have been adequately addressed. Withdrawal of these rejections is requested.

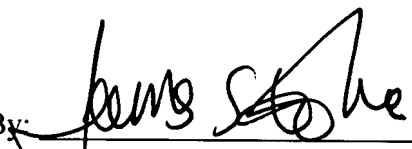
Conclusion

The Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at (650) 833 7723.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number AREN-007CON2.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: November 5, 2007

By: 
James S. Keddie, Ph.D.
Registration No. 48,920

Enclosures: Supplemental Application Data Sheet
Exhibits A and B
IDS citing references A-L, Eigler (J. Leukocyte Biology 1998 63: 101-107), Moore et al (Clin. Exp. Immunol. 1995 101: 387-389) and Benbernou (Immunology 1997 91: 361-368).

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